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EXAMINER	
WANG, CHANG YU	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,294	MICHEL ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 20-53* is/are pending in the application.

4a) Of the above claim(s) *10 and 20-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/31/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-9), IL-6/IL6R-IL6 chimera and O4+ oligodendrocytes in the reply filed on 1/28/2008 is acknowledged. The traversal is on the ground(s) that Groups I-VIII are linked by a special technical feature that makes contribution over the prior art. Applicant argues that the references of Zhang et al. and WO03/059376 are not prior art because the Israeli priority document IL156430 antedates the priority of the cited references. In addition, Applicant argues that the references of Shimazaki et al. and MacDonald et al. do not anticipate the amended claims because the amended claims now recite embryoid bodies (EB) and neurospheres (ES) derived from embryonic stem (ES) cells, which are different from neural stem cells derived from embryos or CNS fetal cells. Applicant's arguments have been fully considered but they are not persuasive because even though claim 1 has been amended, the references of Shimazaki et al. and MacDonald et al. still anticipate the 1st claim. As previously made of record, Shimazaki et al. and MacDonald et al. disclosed a method of generating oligodendrocytes comprising culturing embryonic stem cells in the presence of CNTF and that cells are originally derived from embryonic stem cells because the cells of Shimazaki and MacDonald are from embryos and stem cells or neural stem cells derived from embryos are also embryonic stem cells. Thus, claim 1 is anticipated by Shimazaki et al. and MacDonald et al.. Since the 1st claimed invention has no special technical feature, it cannot share a special technical feature with the other claimed inventions. Thus, Applicant's inventions lack unity of invention

because they do not have a single inventive concept and do not share a special technical feature that contributes over the prior art.

Upon reconsideration, the species election on cytokine and oligodendrocyte is withdrawn. Thus, the subject matter to the extent of CNTF, OSM, IL-11 and O1+ oligodendrocytes are included and under examination in this office action.

The requirement of the rest of the restriction is still deemed proper and is therefore made FINAL.

2. Claims 11-19 are canceled. Claims 1-10 and 20-53 are pending. Claim 1 is amended. Claims 10 and 20-53 are withdrawn with traverse from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1-9 are under examination in this office action.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The elected invention is directed to a method of generating oligodendrocytes from embryonic stem cells in the presence of gp130 activators including CNTF, OSM, IL-6, IL-6/IL6R chimera and IL-11.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of generating oligodendrocytes comprising growing embryonic stem cells (ES), embryoid bodies (EB) and/or neurosphere (ES) cells from ES cells in the presence of one or more gp130 activators selected from CNTF, OSM, IL-6, IL6R/IL6 chimera and IL-11 to differentiate ES, EB or ES cells into $O4^+$ or $O4^+O1^+$ oligodendrocytes in cultures, does not reasonably provide enablement for the above method of generating oligodendrocytes suitable for repairing damage caused by any demyelinating disease as currently claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

"There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the

enablement requirement and whether any necessary experimentation is 'undue'. These factors include, but are not limited to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)". See MPEP § 2164.01.

Breadth of the claims: The claims are directed a method of generating oligodendrocytes suitable for repairing damage caused by demyelinating diseases comprising growing embryonic stem cells (ES), embryoid bodies derived from ES, neurosphere (NS) cells derived from ES cells in the presence of one or more gp130 activators selected from CNTF, OSM, IL-6, IL6R/IL6 chimera and IL-11. The claims encompass generating differentiated or mature oligodendrocytes *in vitro* and also encompass preparing or harvesting differentiated or mature oligodendrocytes *in vitro* for repairing damage caused by all forms of demyelinating diseases.

Nature of the invention: The instant invention is based on Applicant's observation on differentiation of cultured embryonic stem cells, embryoid bodies and or neurosphere cells from ES into $O4^+$ or $O4^+O1^+$ oligodendrocytes in the presence of IL6/IL6R chimera in vitro. Applicant extrapolates the finding to a method of generating oligodendrocytes suitable for repairing damage caused by all forms of demyelinating diseases. However, no data or *in vivo* data is provided to demonstrate that mature or

differentiated oligodendrocytes prepared from the claimed method can be used in repairing any damage caused by any demyelinating diseases.

State of the prior art/predictability/experimentation: Based on the prior art and the specification, Applicant is enabled for a method of generating or differentiating oligodendrocytes in vitro from cultured embryonic stem cells, embryoid bodies and neurospheres from ES cells in the presence of a gp130 activator including CNTF, OSM, IL-6, IL6/IL6R chimera and IL-11. However, the claims are not limited to differentiating or generating oligodendrocytes with a gp130 activator *in vitro*. Rather, the instant claims encompass preparation of oligodendrocytes suitable for repairing all forms of damage caused by all forms of demyelinating diseases. However, Applicant fails to provide sufficient guidance as to enable a skilled artisan to practice the claimed invention as currently claimed because the claims encompass testing differentiated or mature oligodendrocytes for regeneration from a mature damaged neuron of the CNS *in vivo* and also encompass testing nerve or neurite regeneration of the CNS *in vivo* using mature or differentiated oligodendrocytes.

First, neither the specification nor the prior art demonstrates that the differentiated oligodendrocytes that have already formed myelin sheaths can be isolated from a culture dish without damaging the myelin sheaths and also without damaging the cultured oligodendrocytes or to keep the isolated oligodendrocytes alive and functional to repair another damaged mature neurons. It is known in the art that differentiated oligodendrocytes in cultures have already developed myelin sheaths that attached to the culture dish. It would require a skilled artisan to trypsinize or use a mechanic force

to isolate the attached differentiated oligodendrocytes from the culture dish. However, neither the prior nor the specification has taught such method without damaging the oligodendrocytes.

Second, neither the specification nor the prior art demonstrates that the differentiated oligodendrocytes isolated from dishes can be used and also can repair any damage caused by any demyelinating disease. It is known in the art that the regeneration in the central nervous system is still a challenge. Several molecules have been identified to inhibit remyelination in the CNS and axonal/neurite regeneration, myelin-associated molecules such as Nogo, MAG, and proteoglycans in the extracellular matrix, (see p. 1052, 2nd col., Blight Nat. Neurosci. 2002. 5: 1051-4; p. 316, Schmidt et al. Annu. Rev. Biomed. Eng. 2003. 5: 293-347 and p. 450, 2nd col. Hoke et al. Nat. Clin. Pract. Neurol. 2006: 448-454). The nerve injury of the CNS in vivo results in generation of glial scars, which inhibits nerve regeneration of the CNS (Hoke et al. Nat. Clin. Pract. Neurol. 2006: 448-454). Neither the specification nor the prior art teaches that degeneration of the CNS *in vivo* or a lesioned CNS mature neuron *in vitro* can be regenerated by any given agent or a mature or differentiated oligodendrocyte as currently claimed.

Based on the specification and the prior art, Applicant is enabled for generating oligodendrocytes from cultured ES, EB and/or NS cells in the presence of a gp130 activator CNTF, OSM, IL-6, IL6/IL6R chimera and IL-11 *in vitro*. Applicant may predictably be able to induce oligodendrocyte differentiation from endogenous neural stem cells with a gp130 activator *in vivo* while neural development occurs during the

embryonic neural development stage. However, the claims are not limited to the in vitro method as set forth above. The claims are directed to preparing differentiated oligodendrocytes from ES cells or EB or NS cells with the treatment of a gp130 activator *in vitro* because EB and NS cells only occur in an *in vitro* condition not *in vivo*. The claims are also directed to preparing and determining differentiated oligodendrocytes for repairing any damage caused by any demyelinating diseases, which is not enabled. Applicant is not enabled for regenerating an axon of a mature lesioned neuron of the CNS *in vivo* caused by any forms of damages or diseases using a differentiated or mature oligodendrocyte as recited in instant claims 1-9 because neither prior art nor the specification has provided any evidence that the nerve damage of the CNS or a lesion CNS axon of a mature neuron can be repaired by a differentiated or mature oligodendrocyte isolated from a dish even though the isolated differentiated/mature oligodendrocyte is still alive. Applicant is not enabled for the instant invention without undue experimentation since neither prior art nor the specification has provided any evidence that differentiated or mature oligodendrocyte can be isolated from culture dishes without damage and further can be used to repair any damage of the CNS.

Given the highly unpredictable nature of treating any CNS lesion in any patient with mature or differentiated oligodendrocytes isolated from culture dishes, a skilled artisan cannot be reasonably assured that the disclosed invention would be effective. Moreover, the specification fails to provide adequate guidance for the skilled artisan to overcome the unpredictability and challenges of treating any CNS lesion in animals or human. The instant specification is not enabling because one can not follow the

guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

In addition, claim 2 recites "a mutein, functional derivative, active fraction, and circulatory permutated derivative". However, the specification provides insufficient guidance as to how to make and use the claimed mutein, functional derivative, active fraction, and circulatory permutated derivative. Although the specification provides a general description of these claimed muteins and derivatives, it is simply to invite others to test whether these claimed muteins and derivatives are and to determine whether they can be used in the claimed method. The specification fails to teach what specific common structures, amino acid sequences, or characteristics are required for these claimed muteins and derivatives to maintain the activity of IL6/IL6R chimera. It is known in the art that a single amino acid change can abolish the activity or the binding ability of a molecule. For example, a substitution of lysine residue by glutamic acid at position 118 of acidic fibroblast growth factor results in a substantial loss of its biological activity including the binding ability to heparin and its receptor (Burgess et al. J of Cell Bio. 111:2129-2138, 1990). Although many amino acid substitutions are possible in any given protein, the position of where such amino acid substitutions can be made is critical for maintaining the function of a protein; i.e. only certain positions can tolerate conservative substitutions without changing the relationship of three dimensional structure and function of the protein (col. 2, p. 1306, Bowie et al. Science, 1990, 247:1306-1310). Although the specification outlines art-recognized procedures for

producing and the screening method, this is not adequate guidance as to the nature of active muteins and derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would not immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active because conformation is dependent upon surrounding residues; i.e. substitution of non-essential residues can often destroy activity. In addition to a core determinant sequence, the protein-protein interaction also relies on the flanking or noncontiguous residues (see p. 445 the second column, first paragraph, Pawson et al. 2003, Science 300:445-452). The optimal binding motif for a domain is not necessarily suitable for physiological or in vivo interaction. The predictive data always need to be validated by actual analyses in cells (see p. 445, the third column, second paragraph, Pawson et al. 2003, Science 300:445-452).Thus, a skilled artisan cannot contemplate what these muteins and derivatives are and whether they can be used in the claimed method.

Therefore, in view of the complex nature of the invention, the lack of working example and guidance in the specification, the unpredictability of the claimed methods, the current status of the prior art and the breadth of the claims, undue experimentation would be required by a skilled artisan to practice the claimed invention as it pertains to a method of generating oligodendrocytes suitable for repairing damage caused by demyelinating diseases comprising growing embryonic stem cells (ES), embryoid bodies derived from ES, neurosphere (NS) cells derived from ES cells in the presence

of one or more gp130 activators selected from CNTF, OSM, IL-6, IL6R/IL6 chimera and IL-11.

6. Claim 2 is also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claim 2 is drawn to a method of generating oligodendrocytes suitable for repairing damage caused by demyelinating diseases comprising growing embryonic stem cells (ES), embryoid bodies derived from ES, neurosphere (NS) cells derived from ES cells in the presence of a gp130 activator wherein the activator is an IL6/IL6R chimera, a mutein, functional derivative, active fraction, circulatory permutated derivative or salt thereof. The claims encompass use of a genus of mutein, a genus of functional derivative, a genus of active fraction, and a genus of circulatory permutated derivative of IL6/IL6R chimera. Applicant has not disclosed sufficient species for the

broad genus of mutein, of functional derivative, of active fraction, and of circulatory permutated derivative. The specification only describes an IL6/IL6R chimera to be used in the claimed method. However, the claims are not limited to the IL6/IL6R chimera as set forth above but also include structurally and functionally undefined muteins, functional derivatives, active fractions, and circulatory permutated derivatives of IL6/IL6R chimera.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant is in possession of and what Applicant is claiming. From the specification, it is clear that Applicant is in possession of an IL6/IL6R chimera that can be used in the claimed method. Although the specification describes several possible muteins and derivatives on p. 17-24 of the specification, Applicant is not in possession these muteins and derivatives as described in the specification to be used in the claimed method. There is no identification of any particular portion of the structure that must be conserved. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of muteins and derivatives. There is no description of the conserved regions which are critical to the function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure of the muteins and derivatives to the IL6/IL6R chimera function. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the muteins and derivatives might be. Since

the common characteristics/features of the claimed mutein and derivatives are unknown, a skilled artisan cannot envision the functional correlations of the claimed genus with the claimed invention. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genus of proteins.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, a method of generating oligodendrocytes suitable for repairing damage caused by demyelinating diseases comprising use of a gp130 activator wherein the activator is an IL6/IL6R chimera, a mutein, functional derivative, active fraction, circulatory permutated derivative or salt thereof has not met the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement. See MPEP § 2163.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
>
> There are two separate requirements set forth in this paragraph:
> (A) the claims must set forth the subject matter that applicants regard as their invention; and (B) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-9 are indefinite because the term “gp130” and the term “OSM” recited in the claims without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: or providing a full name for abbreviated names. Without identification of property or combination of properties which are unique to and, therefore, definitive of

the instant recitations, the metes and bounds of the claims remain undetermined. Further, the use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. The rejection can be obviated by amending the claims to specifically and uniquely identify gp130, for example, by SEQ ID NO. and function of gp130.

In addition, Claim 2 is indefinite because the claim recites "an IL6R/IL6 chimera, a mutein, functional derivative, active fraction, circularly permutated derivative or salt thereof". The claim is drawn to muteins and derivatives of an IL6R/IL6 chimera. However, the disclosure fails to set forth the metes and bounds of what is encompassed within the definition of such mutein, functional derivative, active fraction, circularly permutated derivative or salt and thus the claim is indefinite.

Further, claim 2 is indefinite because the claim recites a broad limitation and the claim depends from a claim having a narrow limitation. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to

whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 2 recites the broad recitation "the gp130 activator is an IL6R/IL6 chimera, a mutein, functional derivative, active fraction, circularly permutated derivative or salt thereof, and the claim also recites "one or more gp130 activators selected from CNTF, OSM, IL-6, IL6R/IL6 chimera and IL-11", which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9 are rejected under 35 U.S.C. 102 (b) as being anticipated by Nichols et al. (Exp. Cell Res. 1994. 215: 237-239 as in IDS) as evidenced by Baumann et al. (Physol. Rev. 2001. 81:871-927) and Billon et al. (J. Cell Sci. 2002. 115: 3657-3665, as in IDS).

Claims 1-9 are drawn to a method of generating oligodendrocytes suitable for repairing damage caused by demyelinating diseases comprising growing embryonic stem cells (ES), embryoid bodies derived from ES, neurosphere (NS) cells derived from

ES cells in the presence of one or more gp130 activators selected from CNTF, OSM, IL-6, IL6R/IL6 chimera and IL-11. The rejection is based on what is enabled in the instant claims, which are directed to generation of oligodendrocytes from embryonic stem (ES) cells, embryoid bodies (EB) and/or neurosphere (NS) cells from ES in the presence of one or more gp130 activators selected from CNTF, OSM, IL-6, IL6R/IL6 chimera and IL-11.

Nichols et al. teach a method of generating oligodendrocytes comprising growing embryonic stem cells in the presence of a gp130 activator including a IL6/IL6R chimera, CNTF or OSM as recited in instant claims 1-9 (see p. 237, abstract; p. 237, 2nd col-p. 238, 1st col., in particular). Although Nichols et al. do not explicitly teach differentiation of oligodendrocytes in cultured embryonic stem cells in the presence of an IL6/IL6R chimera, CNTF or OSM, the differentiation and generation of oligodendrocytes is an inherent result of treatment of IL6/IL6R chimera, CNTF or OSM to the cultured embryonic stem cells because the steps and materials of the Nichols' method are identical to the claimed method as recited in instant claims.

Although Nichols et al. do not explicitly teach embryoid bodies and neurosphere cells derived from embryonic stem (ES) cells as recited in instant claims 1 and 4-6, it is known in the art embryonic stem cells cultured in the ES culture medium in vitro would form embryoid bodies and neurospheres as evidenced by Billon et al. (see p. 3658, 2nd col., 3rd paragraph-p. 3659, 1st col., 2nd paragraph, in particular, J. Cell Sci. 2002. 115: 3657-3665, as in IDS). Thus, embryoid bodies and neurospheres derived from embryonic stem cells can also found in the cultures of embryonic stem cells.

Although Nichols et al. do not explicitly teach expression $O4^+$ and $O1^+$ markers on differentiated oligodendrocytes as recited in instant claims 7-8, the expression of these markers on differentiated oligodendrocytes is an inherent feature of differentiated oligodendrocytes as evidenced by Baumann et al. (see p. 875, 2nd col, 2nd -3rd paragraphs, in particular, Physol. Rev. 2001. 81:871-927). Baumann teaches that markers of differentiated oligodendrocytes including O4+ and O1+ (see p. 875, 2nd col, 2nd -3rd paragraphs, in particular). Note that

"The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). " See MPEP § 2112.01 [R-3].

In addition, a preamble (i.e. generation of oligodendrocytes) is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations (i.e. growing embryonic stem cells in the presence of IL6/IL6R chimera, CNTF or OSM) are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

In summary, Nichols teaches the same method as the claimed method of the claims 1-9 that are directed to culturing embryonic stem cells in the ES culture medium in the presence of a gp130 activator including IL6/IL6R chimera, CNTF or OSM. The generation of oligodendrocytes, embryoid bodies and neurospheres and the expression of O4 and O1 on differentiated oligodendrocytes are the inherent or intended results of

the claimed methods, which would also occur in the method of Nichols because the steps and materials of the Nichols' method are identical to the instant claims. Therefore, claims 1-9 are anticipated by Nichols et al.

9. Claims 1-9 are rejected under 35 U.S.C. 102 (b) as being anticipated by WO01/88104 (Carpenter. published Nov 22, 2001) as evidenced by Baumann et al. (Physol. Rev. 2001. 81:871-927).

Claims 1-9 are drawn to a method of generating oligodendrocytes suitable for repairing damage caused by demyelinating diseases comprising growing embryonic stem cells (ES), embryoid bodies derived from ES, neurosphere (NS) cells derived from ES cells in the presence of one or more gp130 activators selected from CNTF, OSM, IL-6, IL6R/IL6 chimera and IL-11. The rejection is based on what is enabled in the instant claims, which are directed to generation of oligodendrocytes from embryonic stem (ES) cells, embryoid bodies (EB) and/or neurosphere (NS) cells from ES in the presence of one or more gp130 activators selected from CNTF, OSM, IL-6, IL6R/IL6 chimera and IL-11.

WO01/88104 teaches a method of differentiating oligodendrocytes comprising growing primate pluripotent stem (pPS) cells including human embryonic stem cells in the presence of a gp130 activator including LIF, CNTF and IL-6 as recited in instant claims 1-9 (see p. 3; p. 6; p.8, lines 2-p. 11; p. 19, lines 10-35 examples, in particular). WO01/88104 teaches embryoid bodies and neurosphere cells (i.e. are also name embryoid bodies) derived from embryonic stem (ES) cells as recited in instant claims 1

and 4-6 (see p. 19, lines 10-35, in particular). Thus, embryoid bodies and neurospheres derived from embryonic stem cells can also found in the cultures of embryonic stem cells.

Although WO01/88104 does not explicitly teach expression $O4^+$ and $O1^+$ markers on differentiated oligodendrocytes as recited in instant claims 7-8, the expression of these markers on differentiated oligodendrocytes is an inherent feature of differentiated oligodendrocytes as evidenced by Baumann et al. (see p. 875, 2nd col, 2nd -3rd paragraphs, in particular, Physol. Rev. 2001. 81:871-927). Baumann teaches that markers of differentiated oligodendrocytes including O4+ and O1+ (see p. 875, 2nd col, 2nd -3rd paragraphs, in particular). Note that for the reasons as set forth above, the discovery of a previously unappreciated property (i.e. expression of O4 and O1 on differentiated oligodendrocytes) does not render the claimed property patentable.

In addition, a preamble (i.e. generation of oligodendrocytes) is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations (i.e. growing embryonic stem cells in the presence of IL6/IL6R chimera, CNTF or OSM) are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

In summary, WO01/88104 teaches the same method as the claimed method of the claims 1-9 that are directed to culturing embryonic stem cells in the ES culture medium in the presence of a gp130 activator including LIF, CNTF and IL-6. The

generation of oligodendrocytes, embryoid bodies and neurospheres and the expression of O4 and O1 on differentiated oligodendrocytes are the inherent or intended results of the claimed methods, which would also occur in the method of WO01/88104 because the steps and materials in the method of WO01/88104 are identical to the instant claims. Therefore, claims 1-9 are anticipated by WO01/88104.

10. Claims 1-9 are rejected under 35 U.S.C. 102 (b) as being anticipated by US Patent No. 6562619 (Gearhart et al. issued on May 13, 2003, priority Mar 31, 1998) as evidenced by Baumann et al. (Physol. Rev. 2001. 81:871-927).

Claims 1-9 are drawn to a method of generating oligodendrocytes suitable for repairing damage caused by demyelinating diseases comprising growing embryonic stem cells (ES), embryoid bodies derived from ES, neurosphere (NS) cells derived from ES cells in the presence of one or more gp130 activators selected from CNTF, OSM, IL-6, IL6R/IL6 chimera and IL-11. The rejection is based on what is enabled in the instant claims, which are directed to generation of oligodendrocytes from embryonic stem (ES) cells, embryoid bodies (EB) and/or neurosphere (NS) cells from ES in the presence of one or more gp130 activators selected from CNTF, OSM, IL-6, IL6R/IL6 chimera and IL-11.

US Patent No. 6562619 (the '619 patent) teaches a method of differentiating oligodendrocytes comprising growing embryonic stem (pPS) cells including mouse and human embryonic stem cells in the presence of a gp130 activator including IL-6 and IL-11 as recited in instant claims 1-9 (see col. 28, example 6; col. 30, claims 1-28, in

particular). The '619 patent also teaches embryoid bodies and neurosphere cells derived from embryonic stem (ES) cells as recited in instant claims 1 and 4-6 (see co.. 29, lines 29-40; col.30, claim 9). Thus, embryoid bodies and neurospheres derived from embryonic stem cells can also found in the cultures of embryonic stem cells. In addition, the '619 patent teaches expression $O4^+$ and $O1^+$ markers on differentiated oligodendrocytes from embryonic stem cells or EB or NS cells as recited in instant claims 7-8 (see col 14, line 27-col. 15, line 4). Further, the expression of these markers on differentiated oligodendrocytes is an inherent feature of differentiated oligodendrocytes as evidenced by Baumann et al. (see p. 875, 2^{nd} col, 2^{nd} -3^{rd} paragraphs, in particular, Physol. Rev. 2001. 81:871-927). Baumann teaches that markers of differentiated oligodendrocytes including O4+ and O1+ (see p. 875, 2^{nd} col, 2^{nd} -3^{rd} paragraphs, in particular). Note that the discovery of a previously unappreciated property (i.e. expression of O4 and O1 on differentiated oligodendrocytes) does not render the claimed property patentable.

"The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). " See MPEP § 2112.01 [R-3].

In addition, a preamble (i.e. generation of oligodendrocytes) is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations (i.e. growing embryonic stem cells in the presence of IL6 or IL-11) are able to stand alone.

See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

In summary, The '619 patent teaches the same method as the claimed method of the claims 1-9 that are directed to culturing embryonic stem cells in the ES culture medium in the presence of a gp130 activator including IL6 and IL-11. The generation of oligodendrocytes, embryoid bodies and neurospheres and the expression of O4 and O1 on differentiated oligodendrocytes are the inherent or intended results of the claimed methods, which would also occur in the method of the '619 patent because the steps and materials in the method of the '619 patent are identical to the instant claims. Therefore, claims 1-9 are anticipated by the '619 patent.

Conclusion

11. NO CLAIM IS ALLOWED.

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.
WO02/086073 (Studer et al., published Oct 31, 2002) teaches a method of generating oligodendrocytes from embryonic stem cells in the presence of CNTF.

13. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
April 21, 2008

/Christine J Saoud/
Primary Examiner, Art Unit 1647